UNIVERSITY OF UTAH COLLEGE OF PHARMACY

FINAL READING APPROVAL

TO THE DOCTOR OF PHARMACY COMMITTEE OF THE UNIVERSITY OF UTAH COLLEGE OF PHARMACY:

I have read the clinical research project report of Edgar R. Gonzalez in its final form and have found that 1) its format, citations, and bibliographic style are consistent and acceptable; 2) its illustrative materials including figures, tables, and charts are in place; and 3) the final manuscript is satisfactory to the Supervisory Committee and is ready for submission to the Doctor of Pharmacy Committee.

5/19/83
Date

Chairman, Supervisory Committee

Approved for the Department of Pharmacy Practice

Chairman

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Chairman, Doctor of Pharmacy Committee

UNIVERSITY OF UTAH COLLEGE OF PHARMACY

SUPERVISORY COMMITTEE APPROVAL

of a clinical research project report submitted by

Edgar R. Gonzalez

We, the undersigned, have read this clinical research project report and have found it to be of satisfactory quality for a Doctor of Pharmacy Degree.

5/17/83
Date

Chairman, Supervisory Committee

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A COMPARISON OF PLASMA CONCENTRATION, ARRHYTHMIA RESPONSE, AND ELECTROCARDIOGRAPHIC CHANGES IN PATIENTS REQUIRING QUINIDINE THERAPY

by

Edgar R. Gonzalez

A project submitted to the faculty of the
University of Utah in partial fulfillment of the requirements
for the degree of

Doctor of Pharmacy

College of Pharmacy

University of Utah

May 1983

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INTRODUCTION

Quinidine is a naturally occurring substance used in the treatment of cardiac arrhythmias. It may be administered orally or parenterally to control both ventricular and supraventricular arrhythmias. Because of its low therapeutic index, it is rational to obtain plasma concentrations of quinidine as a guide to the safest and most effective dose. Unfortunately, past studies that were designed to compare plasma quinidine concentration to arrhythmias control and electrocardiographic (ECG) changes used nonspecific assay techniques.[1-6] Such methods can neither completely nor consistently separate quinidine from its metabolites and contaminants which may differ in their myocardial and possibly their toxic effects. Our experience has been that arrhythmia control can often be achieved with plasma quinidine concentrations lower than the reported therapeutic ranges. The availability of a high performance liquid chromatography (HPLC) method provides an opportunity to establish a more accurate therapeutic range using a highly specific assay technique. This has not been adequately studied although it is suggested that therapeutic efficacy may be achieved at a concentration of 1.0[8] or 0.7 mcg/ml.[9]

Investigators have evaluated the effects of quinidine on intraventricular conduction and ventricular repolarization.[4,6] In 1970, Heissenbuttel et al,[4] employed the nonspecific fluorometric assay described by Brodie and Udenfriend to determine the plasma quinidine concentration in 20 patients started on oral quinidine and monitored

for three days. Within the range of 2 to 5 mcg/ml, quinidine caused a significant increase in the duration of the QRS complex and the QT interval on the electrocardiogram. Furthermore, widening of the QRS complex was directly proportional to increases in the plasma quinidine concentration. A recent study by Holford et al,[6] examined the relationships between electrocardiographic readings, systolic time interval measurements and changes in the plasma quinidine concentration. The plasma concentrations were determined in 10 normal subjects. The major effect of quinidine was slowing of cardiac repolarization; this was supported by their observation of prolongated QT intervals. Holford et al,[6] noted small increases in the PQ interval and the QRS complex. To date, there are no published reports comparing quinidine concentrations assayed by the specific HPLC assay with concurrent ECG changes in patients requiring chronic antiarrhythmic therapy.

This study examined the relationship between HPLC-derived plasma quinidine concentrations, arrhythmia control and simultaneous six lead ECG measurements in patients requiring antiarrhythmic therapy.

Study Objectives

1. Evaluate the correlation between the independent variable (plasma quinidine concentration) and the dependent variables (changes in the QRS complex and the QT interval) and determine if these electrocardiographic measurements can be used as reliable predictors of the patients' plasma quinidine concentration.

2. Determine if the changes in the QRS complex and the QT interval occur at the same quinidine concentration or if the changes in one ECG parameter occur at a lower quinidine concentration than the changes in the other.

3. Evaluate differences between responders and nonresponders to quinidine therapy by comparing the mean plasma concentration, mean changes in the ECG parameters in the two groups. Therapeutic response was determined at steady state quinidine concentrations.

MATERIALS AND METHODS

Patient Selection

Inclusion Criteria: Patients, 18 years of age or older, who required antiarrhythmic therapy and have signed an informed consent were admitted to the study. Patients were located at the University Hospital Coronary Intensive Care Unit or 4 North Telemetry Unit.

Exclusion Criteria: A patient was excluded from the study if at the start of the study or throughout the course of the study the patient met any of the following criteria:

1. Hypersensitivity reaction to quinidine, quinine, or other cinchona alkaloids.
2. Side effects experienced by the patient which in the opinion of the attending physician warranted discontinuation of the drug, e.g., gastrointestinal intolerance, tinnitus, hemolytic anemia.
3. Concomitant use of any of the following antiarrhythmic agents (procainamide, disopyramide, phenytoin, and verapamil). This included any period of time less than 5 half-lives between discontinuation of the agent and the start of quinidine therapy.
4. Concomitant use of tricyclic antidepressants, phenothiazines, or other psychotherapeutic agents excluding the benzodiazepine derivatives.
5. Serum potassium concentrations that continually vary from the normal range (3.5-5.0 mEq/L).
6. Pregnancy determined by the patient's history.

7. Concomitant use of any of the following hepatic microsomal enzyme inducing agents: barbiturates, phenytoin, rifampin, griseofulvin, or glutethimide within four weeks of starting quinidine therapy.

Electrocardiographic Measurements

All ECG measurements in this study were obtained from a standard six-lead (I, II, III, AVR, AVL, and AVF) electrocardiogram recorded on a Hewlett-Packard 1515 B Automatic Cardiograph at a paper speed of 50 mm/sec. All ECG tracings were performed with the patients in the supine position. The ECG lead yielding the widest QRS complex was used to measure the QRS complex for that ECG tracing. Five separate measurements were obtained from each tracing by the same two cardiology residents who were unaware of the patients' plasma quinidine concentrations. The ten observations were averaged. The same procedure was repeated for the QT interval determinations. Bazzett's formula[10] ($QT_c = QT/\sqrt{R-R}$) was used to correct the QT interval for heart rate. The accuracy in measurement of the QRS complex and QT interval was ± 5 m-sec.

Before the start of quinidine therapy, a baseline six-lead ECG was obtained from all patients entered in the study. This served as the control value for QRS and QT interval determinations.

In order to evaluate therapeutic response on the criteria set forth by this protocol, all patients enrolled in the study had constant 24 hour ECG monitoring by Holter monitor or computer programmed telemetry.

Dosing Protocol

Patients received a maintenance dose of 10-14 mg/kg/day of quinidine base administered orally as the sulfate or the gluconate salt as divided doses at six to eight hour intervals.

Blood Sampling Techniques

Peak blood samples (drawn two hours after the oral dose of quinidine sulfate and four hours after the oral dose of quinidine gluconate) and simultaneous six-lead ECG measurements were obtained twice on day one and two, and once on the third day after the start of quinidine therapy.

The blood samples were drawn through an intravenous heparinized catheter. The initial 2 ml of blood were discarded and 7 ml of blood were collected in a collection tube containing sodium fluoride and potassium oxalate. The samples were centrifuged immediately and the plasma was frozen in silanized teflon cap, screw-type culture tubes.

Analytical Method[7]

Plasma quinidine determinations were performed in the Clinical Toxicology Laboratory of the University of Utah Hospital. The assay employed was the HPLC method described by Bridges et al[7] for simultaneous quantitation of quinidine, procainamide, N-acetylprocainamide, and disopyramide. This assay had a sensitivity limit of 0.5 mcg/ml and a coefficient of variation for identical samples of less than four percent.

Data Analysis[11]

The relationship between the changes in the QRS complex and the QT interval from control values (Δ QRS and Δ QT) and the plasma quinidine concentration (mcg/ml) was plotted on a scattergram. A least squares line of best fit obtained. Linear regression analysis was used to determine if electrocardiographic measurements could be used as reliable predictors for plasma quinidine concentration.

Student's t-test was used to evaluate the difference between the mean plasma concentration required to produce greatest change from baseline for each of the ECG parameters.

A patient was deemed a responder if either or both of the following criteria were met:[12]

1. conversion to normal sinus rhythm after the start of quinidine therapy in patients with atrial fibrillation or atrial flutter
2. complete suppression of ventricular premature beats (VPB) for one-half hour, or 90 percent suppression for at least two consecutive half-hour segments of the dosing interval in patients with ventricular dysrhythmias when compared to baseline.

RESULTS

Preliminary data were obtained from four patients who completed the study. All four patients met all criteria set forth by the protocol. The mean age of the patients was 71 years (Table I). The four subjects had a normal baseline CBC, platelets, arterial blood gases, and serum potassium measurements.

A total of 17 simultaneous six-lead electrocardiograms and blood samples were obtained from the four patients (Table II). The change

in the QRS complex (Δ QRS) and the change in the rate-corrected QT interval (Δ QT_c) were plotted as a function of the plasma quinidine concentration (Figures A and B). The Pearson product moment correlation coefficient showed a linear relationship ($p < 0.01$) between the changes in the dependent variables and the plasma quinidine concentration. The slope of the regression line for each graph is significantly different from zero ($p < 0.01$).

Table III lists the control values and the maximum values for the QRS complex and the QT_c interval for the study group. Eight percent and four percent change from baseline were considered significant changes ($p < 0.05$) for the QRS complex and QT_c interval, respectively. There was a significant difference between control value and maximum recorded ECG parameter reading for each patient ($p < 0.05$).

Table IV lists the plasma concentrations that produced the greatest change from baseline for each of the ECG parameters. There was no significant difference ($p > 0.05$) between the plasma concentration yielding the greatest change in the QRS complex and QT_c interval for the sample.

Two of the four patients (patients 1 and 4) responded to quinidine therapy. Patient one suffered from a recent onset of frequent multifocal premature ventricular depolarizations and coarse atrial fibrillation with a rapid ventricular response. The patient was started on quinidine and digoxin resulting in conversion to normal sinus rhythm. A 24 hour Holter recording obtained before discharge was compared to the pretreatment 24 hour Holter recording; a marked reduction in the frequency and the complexity of ventricular arrhythmias was noted. The average estimated premature ventricular depolarization had been reduced

from 20 per hour to 16 per hour. Couplets were rare, and triplets and four-beat runs of ventricular tachycardia had been abolished. The patient did not report any quinidine side effects.

Patient four had a history of heart failure for which she was being treated with digoxin and furosemide; the patient was admitted to University Hospital when she developed atrial fibrillation with a rapid ventricular response. The patient was placed on quinidine and converted to normal sinus rhythm within 24 hours after the start of quinidine therapy and has remained in normal sinus rhythm.

Patients two and three failed to respond to quinidine therapy. Both subjects suffered from frequent complex premature ventricular beats which based on 24 hour Holter monitoring did not decrease from baseline after quinidine therapy which produced serum concentrations within the range of 2-5 mcg/ml. These patients were unable to tolerate higher doses of quinidine due to gastrointestinal disturbances caused by the drug.

Only minimal differences were found in the mean plasma, quinidine concentration or the mean changes in the electrocardiographic parameters between responders and nonresponders, Tables V, VI, VII.

DISCUSSION

In man, the most prominent electrocardiographic effect of quinidine at therapeutic plasma concentrations appears to be prolongation of the QT interval without widening of the QRS complex.[13,14] Antiarrhythmic effects of quinidine have been reported when QT prolongation occurred without notable effects on the duration of the QRS complex.[15] Widening of the QRS complex has been considered a late effect seen when

high plasma concentrations of quinidine are achieved.[13] Heissenbuttel and Bigger,[4] suggested that failure to recognize QRS widening at low quinidine concentrations might be due to an inability to recognize the small changes that occur in the width of the QRS complex when measured on the standard electrocardiographic tracing sensitive only to ± 20 m-sec. By using an oscilloscopic time expanded display to enhance horizontal amplification of the ECG parameter, these authors found that quinidine significantly prolonged the duration of the QRS complex at serum concentrations as low as 2 mcg/ml. Significant changes in both the QRS complex and the rate-corrected QT interval correlated with plasma quinidine determinations within the range of 2-5 mcg/ml determined by the method of Brodie and Udenfriend.[4] More recently, Holford et al[6] administered single doses of quinidine to ten normal volunteers and correlated the changes in the QRS complex and the rate-corrected QT interval with plasma quinidine concentrations determined by HPLC assay. Using standard electrocardiographic techniques, these researchers found a significant correlation between the QT interval and plasma concentration within the range of 1-3 mcg/ml while no correlation was found between the QRS complex and plasma concentration.

There are no published reports comparing quinidine concentrations determined by the HPLC assay with concurrent electrocardiographic changes in patients requiring chronic antiarrhythmic therapy. This study examined the relationship between HPLC-derived plasma quinidine concentrations, arrhythmia control and simultaneous six-lead electrocardiographic measurements in patients requiring quinidine therapy, to

determine therapeutic range for quinidine and to devise a non-invasive monitoring technique for quinidine therapy.

The linear regression analysis revealed a significant correlation between the ECG parameters and the plasma quinidine concentration for the patients in this study. The slope of the regression line demonstrated that the dependent variables change as a function of the quinidine concentration within the range of 1.1-4.8 mcg/ml. These results are consistent with the findings of Heissenbuttel and Bigger,[4] and may reflect the more precise electrocardiographic method used. The heightened sensitivity of measurement (± 5 m-sec) allowed for the detection of 8-43 m-sec changes in the ECG measurements. It should be emphasized that the greater accuracy of measurement was achieved by doubling the speed of the ECG recording to enhance the horizontal amplification of the QRS complex and QT interval and by using an ECG caliper rule to perform the measurements. This technique is feasible in most hospitals and clinics in the United States.

The lower range of plasma concentrations reported in this study compared to reports of other similar studies[4,13,14] can be explained by the difference in the assay used. The nonspecific assays used by previous researchers cannot adequately separate quinidine from its impurity and its polar metabolites. A 20-50 percent increase in concentration above the "true" quinidine concentration has been reported when nonspecific assays are compared to HPLC quinidine determinations.[16]

The utility of the QRS complex and the rate-corrected QT interval in assessing therapeutic response and potential toxicity deserves further examination. In this study, a 64 percent widening of the QRS complex was seen in patient two at a serum concentration of 2.8 mcg/ml;

a quinidine concentration of 4.5 mcg/ml produced a 54 percent change in the QRS complex in patient one. Visual inspection of the 95 percent confidence interval in Figures A and B readily discloses the wide range of values in the ECG measurements corresponding to a given quinidine concentration. These findings contradict those previously reported in the literature.[13-15] This may be due to the small number of subjects in this report.

Lyon and DeGraff[15] have postulated that the antiarrhythmic effects of quinidine are seen when QT prolongation occurs without notable effects on the duration of the QRS complex. Based on this statement one would expect that the maximum prolongation of the rate-controlled QT interval would occur at a lower quinidine concentration when compared to maximum widening of the QRS complex. However, in this study, no significant difference ($p > 0.05$) was found between the plasma concentration causing the greatest degree of change in each of the ECG parameters. Once again, these findings are consistent with the data by Heissenbuttel and Bigger and may reflect the similar method employed in measuring ECG changes.

Assessing antiarrhythmic response is controversial because there is marked spontaneous variability in the incidence of ectopic activity from one hour to the next, from one 24 hour Holter monitor to another.[17] Furthermore, there appears to be an even greater spontaneous variability in ventricular premature beat complexity than in the frequency of these ectopic beats.[10]

Based on the stringent criteria for therapeutic response used in this study, there was a 50 percent response rate within the range of 0.75-6.6 mcg/ml of quinidine in plasma, but no differences were

observed between responders and non-responders when plasma quinidine concentration, QRS complex widening, and prolongation of the rate-corrected QT interval were compared. Similar results have been observed by other investigators (Ueda CT, personal communication) who have tried to discern differences in the plasma concentrations between responders and non-responders to quinidine therapy. These findings raise the question of whether response occurred as the result of the added antiarrhythmic effects of the polar metabolites of quinidine. Drayer et al[18] have demonstrated that quinidine, 3-hydroxyquinidine (3-OH) and 2'-oxoquinidinone (2'-OXO) were equally potent antiarrhythmic drugs when tested against chloroform and hypoxia-induced ventricular fibrillation in mice. They also found large interpatient variation in the plasma concentration of the 3-OH and 2'-OXO metabolites in patients on long term quinidine therapy. It is possible that the metabolites accumulate in some patients and contribute to the antiarrhythmic effect of quinidine.[18]

To date no study has focused on the antiarrhythmic activity of quinidine metabolites in man. A study comparing the concentration of quinidine and its metabolites in plasma of patients with therapeutic response versus patients who fail to respond or develop quinidine toxicity would seem warranted.

CONCLUSION

The data evaluated in this study were obtained from only four patients. The few patients reflect the strict criteria required if this type of study is to be valid. Adding to the problem of small sample size was the apparently large interpatient variability in

electrocardiographic changes measured in this study. Even though some of our findings are consistent with previous reports and various observations are statistically significant, these data should be interpreted as trends and should not be extrapolated to the general population. A study to confirm our findings in a larger number of patients and to evaluate the antiarrhythmic activity of the metabolites of quinidine is indicated.

TABLES

Table I. Age of Study Subjects, Type of Arrhythmias Treated and Baseline Values for the ECG Parameters

Patient No.	Age (Yrs)	Arrhythmia	Baseline QRS ± S.D. (Msec)	Baseline QT_C ± S.D. (Msec)	Response to Quinidine
1	66	PVC	79 ± 4.2	400 ± 5.6	Yes
2	80	PVC	62 ± 4.5	436 ± 8.9	No
3	67	PVC	106 ± 8.9	396 ± 25.0	No
4	70	Atrial Fib	61 ± 2.2	412 ± 6.8	Yes
Mean (± S.D.)	71		77 ± 23.51	411 ± 18	

The mean value for the population's age and baseline ECG values are listed on the bottom row. The response column indicates the outcome of quinidine therapy based on the criteria stated in the protocol.

Table II. ECG Recordings and Plasma Quinidine Determinations From the Four Subjects

Patient No.	Sample No.	Cp Quinidine (mcg/ml)	$\bar{X}$ QRS±SD (Msec)	Δ QRS (Msec)	$\bar{X}$ QT_c±SD (Msec)	Δ QT_c (Msec)
1	1	4.50	122 ± 2.7	43	566 ± 5.6	166
1	2	3.50	97 ± 4.5	18	461 ± 2.9	61
1	3	6.60	119 ± 2.2	40	450 ± 3.2	50
1	4	3.20	120 ± 3.5	41	501 ± 2.7	101
1	5	4.80	108 ± 2.7	29	530 ± 5.2	130
1	6	4.05	111 ± 5.5	32	549 ± 2.6	149
2	7	1.30	72 ± 7.6	10	462 ± 7.2	26
2	8	1.10	93 ± 7.6	31	499 ± 1.1	63
2	9	1.40	94 ± 4.2	32	441 ± 1.0	5
2	10	3.00	91 ± 6.5	29	474 ± 1.0	38
2	11	2.80	102 ± 1.0	40	491 ± 5.3	55
3	12	1.60	110 ± 14.0	4	410 ± 5.6	14
3	13	1.80	114 ± 11.0	8	412 ± 8.0	16
3	14	2.85	136 ± 4.0	30	442 ± 8.3	46
4	15	0.75	70 ± 3.5	9	428 ± 8.4	16
4	16	2.00	71 ± 2.2	10	420 ± 3.9	8
4	17	2.30	83 ± 2.7	22	430 ± 3.2	18

Table III. Control Values and the Maximum Values for the QRS Complex and QT_c Interval for Each Patient

Patient No.	Control QRS ± S.D. (Msec)	Maximum QRS (Msec)	Control QT_c (Msec)	Maximum QT_c (Msec)
1	79 ± 4.2	122 ± 2.7	400 ± 5.6	566 ± 5.6
2	62 ± 4.5	102 ± 1.0	436 ± 8.9	499 ± 1.1
3	106 ± 8.9	136 ± 4.0	396 ± 25.0	442 ± 8.3
4	61 ± 2.2	83 ± 2.7	412 ± 6.8	430 ± 3.2

Table IV. Plasma Concentration at the Time of Greatest Change from Baseline for Each of the ECG Parameters are Listed for Each Patient

Patient No.	CP Quinidine (mcg/ml)	Maximum Change QRS (Msec)	Cp Quinidine (mcg/ml)	Maximum Change QT_c (Msec)
1	4.50	43	4.50	166
2	2.80	40	1.10	63
3	2.85	30	2.85	46
4	2.30	22	2.30	18

Table V. Comparison of Mean Plasma Concentration Between Responders and Non-Responders to Quinidine Therapy

Responders (Patient No.)	$\bar{X}$ Cp Quinidine (mcg/ml)	Non-Responders (Patient No.)	$\bar{X}$ Cp Quinidine (mcg/ml)
1	4.44	2	1.92
4	1.68	3	2.08
$\bar{X}$	3.06		2.00
S.D.	1.95		0.115

Table VI. Comparison of Mean Changes in the QRS Complex Between Responders and Non-Responders to Quinidine Therapy

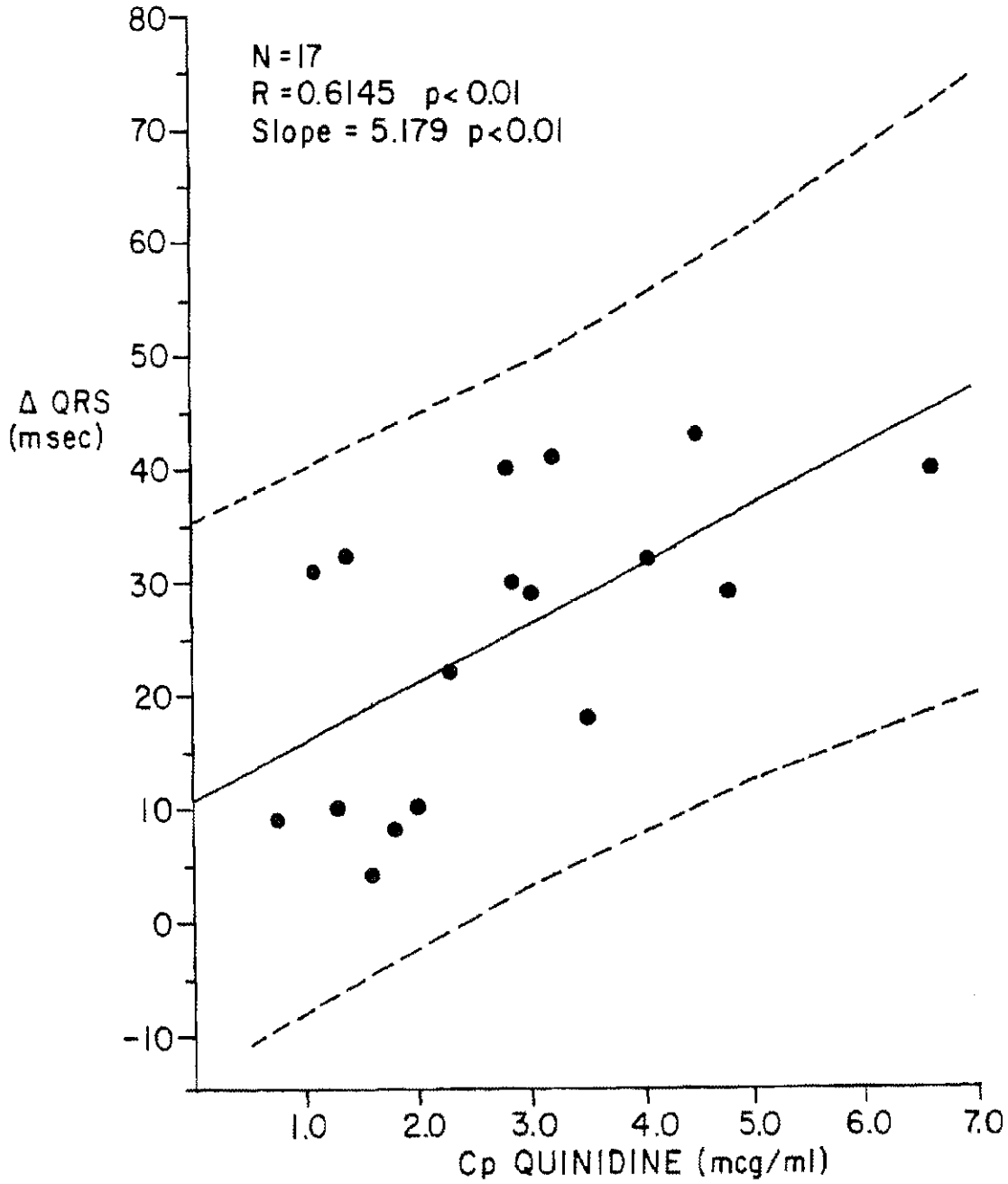
Responders (Patient No.)	Mean Change QRS (Msec)	Non-Responders (Patient No.)	Mean Change QRS (Msec)
1	38.83	2	28.40
4	13.67	3	14.00
$\bar{X}$	26.25		21.20
S.D.	17.79		10.18

Table VII. Comparison of Mean Changes in the QT_c Interval Between Responders and Non-Responders to Quinidine Therapy

Responders (Patient No.)	Mean Change QT_c (Msec)	Non-Responders (Patient No.)	Mean Change QT_c (Msec)
1	109.50	2	33.40
4	14.00	3	25.30
$\overline{X}$	61.75		29.35
S.D.	62.53		5.727

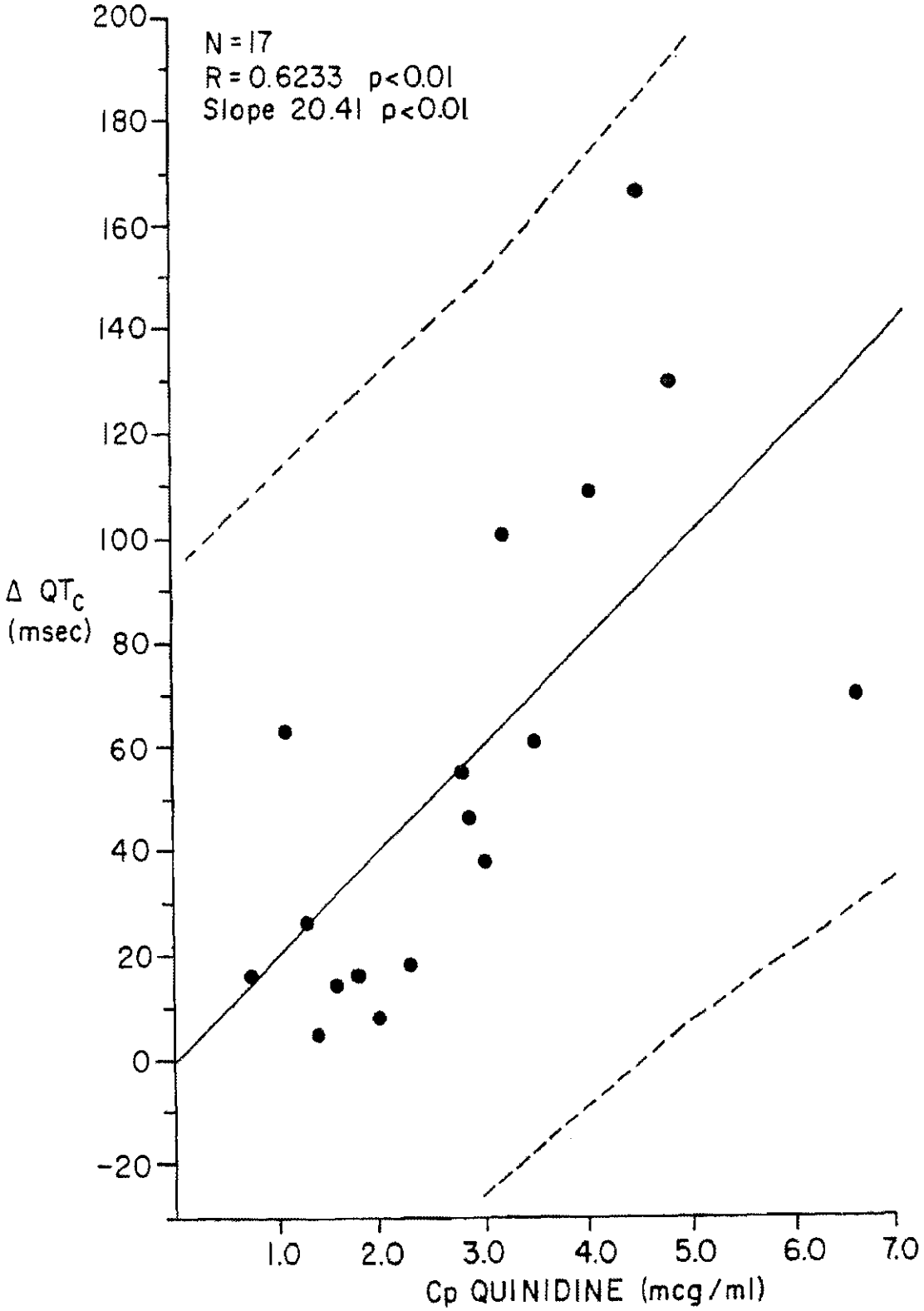
FIGURES

Figure A. Relationship Between Change in QRS Duration From Control Values in Milliseconds (Δ QRS) and Plasma Quinidine Concentration in mcg/ml for the Study Sample



The calculated regression line and the 95 percent prediction interval (broken line) are shown. The change in QRS duration noted in the measurement is dependent on plasma quinidine concentration (slope = 5.179, $p < 0.01$)

Figure B. Relationship Between Change in Rate-Corrected QT Interval From Control Values in Milliseconds (ΔQT_C) and Plasma Quinidine Concentration in mcg/ml for the Study Sample



The calculated regression line and the 95 percent prediction interval (broken line) are shown. The change in the QT_C interval noted in these measurements is dependent on plasma quinidine concentration (slope = 20.41 $p < 0.01$)

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Department of Pharmacy Practice
University of Utah Medical Center
August 1981 - June 1983

Responsibilities: Clinical Rotations (medical team member, daily patient care rounds, monitoring patient therapy, performing medication histories, providing pharmacokinetic and drug therapy selection, teaching inservices, and pharmacy rounds with first year Pharm.D. candidates and undergraduate pharmacy students)

Night Call (drug information service, toxicology information, cardiac arrest team member, and patient care responsibility for the University of Utah Poison Control Center)

Clinical Pharmacy Seminars (to faculty members and hospital pharmacists at the University of Utah)

Committee Meetings (Institutional Review Board, Pharmacy and Therapeutics Committee)

Research (see Research in Progress)

PROFESSIONAL EXPERIENCE (continued)

Registered Pharmacist
Thrift Drug Company
Wynnewood, PA
January 1981 - May 1981

Responsibilities: Compounding and dispensing of medications, patient counseling, maintaining patient profiles, and pharmacy management

Pharmacy Intern
Thrift Drug Company
King of Prussia, PA
May 1978 - December 1980

Responsibilities: Compounding and dispensing of medications under the supervision of a registered pharmacist

LICENSURE

Utah - September 1981 - #03512-1701-6
Pennsylvania - March 1981 - #031511-L

RESEARCH AND OTHER CREATIVE WORK

Reviews

Gonzalez ER: Piperacillin - A semisynthetic penicillin with enhanced antipseudomonas activity is admitted to the formulary. Drugs in Patient Care 5(2):5-6, 1982.

Research in Progress

Principal Investigator: A Comparative Analysis of Plasma Concentration, Arrhythmia Response, and QRS Complex and QT Interval Changes in Patients Requiring Quinidine Therapy. Thomas Caine, M.D., and Bryan Finkle, Ph.D., February 1982-present.

Research Assistant: A Prospective Comparison of the Incidence of Thrombocytopenia and/or Hypertransaminasemia in Patients Receiving Either Beef Lung or Porcine Intestinal Mucosal Heparin. John Russo Jr., Pharm.D., George Dukes Jr., Pharm.D., Steven Sanders, Pharm.D., Glenn Warden, M.D., Jeffrey Saffle, M.D., May 1982-present.

A Study of the Pharmacokinetics, Efficacy and Safety of FK 749 (SK&F 88373-Z) in Pediatric Infections. John Russo Jr., Pharm.D., Kelly D. Mutchie, Pharm.D., Manford Gooch, M.D., July 1982-present.

RESEARCH AND OTHER CREATIVE WORK (continued)

Invited Presentations

"New Agents and Therapeutics for 1982: Antianginal Agents" Continuing Education Program, Utah Pharmaceutical Association, Salt Lake City, UT, Nov. 1982.

"Vasodilator Therapy in Chronic Congestive Heart Failure" Pharmacy Conference, Department of Pharmacy, LDS Hospital, Salt Lake City, UT, Oct. 1982.

"Digitalis Glycosides" Nursing Staff Teaching Seminar, Coronary Care Unit, LDS Hospital, Salt Lake City, UT, Aug. 1982.

"Review of Cardiac Electrophysiology and Antiarrhythmic Agents" Medical Intensive Care Unit-Coronary Care Unit, University of Utah Medical Center, Salt Lake City, UT, Aug. 1982.

"Medications Used During Acute Medical Emergencies: Agents, Doses, and Administration" Medical Staff Conference, Handicapped Children's Center, Salt Lake City, UT, July 1982.

"Potential Complications of Ritodrine Hydrochloride in the Management of Preterm Labor" Department of Obstetrics and Gynecology, University of Utah Medical Center, Salt Lake City, UT, July 1982.

"Narcotic Withdrawal in the Pregnant Patient: Management Potential Risk to the Patient and the Fetus" Nursing Conference, Department of Obstetrics and Gynecology, University of Utah Medical Center, Salt Lake City, UT, June 1982.

"Patient Noncompliance: Why It Occurs and How It Can Be Minimized" Team Staffing Conference, Maternal and Infant Care Clinic, Utah Department of Health, Salt Lake City, UT, June 1982.

"Calcium Channel Blocking Agents" Nursing In-Service, Medical Intensive Care Unit-Coronary Care Unit, Salt Lake City, UT, May 1982.

"Recognition and Management of Acute Adrenal Insufficiency" Nursing In-Service, Surgical Intensive Care Unit, University of Utah Medical Center, Salt Lake City, UT, Feb. 1982.

"Pulmonary Care of the Critically Ill Patient" Pharmacologic Intervention" Continuing Education Lecture, American Association of Critical Care Nurses, Salt Lake City, UT, Jan. 1982.

"Food-Drug Interactions" Nursing Staff Teaching Rounds, Hill Haven Nursing Home, Salt Lake City, UT, Sept. 1981.

RESEARCH AND OTHER CREATIVE WORK (continued)

Seminar Presentations

"Abrupt Discontinuation of Antihypertensive Therapy" Clinical Pharmacy Seminar, College of Pharmacy, University of Utah, Salt Lake City, UT, April 1982.

"The Medical Management of Psoriasis" Clinical Pharmacy Seminar, College of Pharmacy, University of Utah, Salt Lake City, UT, Jan. 1982.

"Adriamycin Cardiotoxicity" Clinical Pharmacy Seminar, College of Pharmacy, University of Utah, Salt Lake City, UT, Sept. 1981.

COMMUNITY ACTIVITIES

Volunteer Registered Pharmacist
Health Screening Center
Salt Lake County Aging Services
Salt Lake City, UT
September 1981 - January 1982

Volunteer Registered Pharmacist
Salt Lake County Health Fair
Salt Lake City, UT
March 1982

Pharmacist In-Charge
Hypertension Screening and Monitoring
Community Service Program, Thrift Drug Company
Wynnewood, PA
June 1980 - May 1981

Diabetic Patient Education and Counseling
Thrift Drug Company
Wynnewood, PA
May 1979 - May 1981

PROFESSIONAL SOCIETIES

American Society of Hospital Pharmacists, September 1982 - present
Utah Society of Hospital Pharmacists, September 1982 - present
American Pharmaceutical Association, January 1981 - present
Pennsylvania Pharmaceutical Association, August 1979 - August 1980
Student American Pharmaceutical Association, August 1977 - December 1980